PB88-178926

Health Effects Assessment for Tin and Compounds

(U.S.) Environmental Protection Agency
Cincinnati, OH

May 87

U.S. Department of Commerce
National Technical Information Service
NTIS

PB88-178926

EPA/600/8-88/055
May, 1987

HEALTH EFFECTS ASSESSMENT FOR TIN AND COMPOUNDS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA/600/8-88/055	2.	3. RECIPIENT'S ACCESSION NO. PB88-178916
4. TITLE AND SUBTITLE Health Effects Assessment for Tin and Compounds		5. REPORT DATE May 1987
		6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS		10. PROGRAM ELEMENT NO.
		11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268		13. TYPE OF REPORT AND PERIOD COVERED
		14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES		

16. ABSTRACT

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with specific chemicals or compounds. The Office of Emergency and Remedial Response (Superfund) uses these documents in preparing cost-benefit analyses under Executive Order 12991 for decision-making under CERCLA. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data are available. The interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed. Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, RfD_S or subchronic reference dose, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval. The RfD is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan. For compounds for which there is sufficient evidence of carcinogenicity, q_1^*s have been computed, if appropriate, based on oral and inhalation data if available.

17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 41
	20. SECURITY CLASS (This page) Unclassified	22. PRICE A03 12.95

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with tin and compounds. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the TOXLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to May, 1986. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1979. Mini-Reviews on the Carcinogenicity, Mutagenicity, Teratogenicity and Chronic Toxicity of Selected Compounds. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, RfD_S (formerly AIS) or subchronic reference dose, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used, or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for RfD_S estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure. These values are developed for both inhalation (RfD_{SI}) and oral (RfD_{SO}) exposures.

The RfD (formerly AIC) is similar in concept and addresses chronic exposure. It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980) for a discussion of this concept]. The RfD is route-specific and estimates acceptable exposure for either oral (RfD_O) or inhalation (RfD_I) with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for identifying reportable quantities and the methodology for their development is explained in U.S. EPA (1983).

For compounds for which there is sufficient evidence of carcinogenicity RfD_S and RfD values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980). Since cancer is a process that is not characterized by a threshold, any exposure contributes an increment of risk. For carcinogens, q_1^*s have been computed, if appropriate, based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates presented.

Several chronic and subchronic oral studies have been performed with several inorganic salts of tin. No adverse effects were noted in rats or mice fed diets containing 2000 ppm stannous chloride for 105 weeks in one study (NTP, 1982). An RfD of 0.62 mg/kg/day (43.4 mg/day) was derived from the NOEL in rats in the NTP (1982) study. This RfD is supported by evidence indicating that ordinary dietary levels of tin in humans consuming moderate amounts of canned food range from 1-38 mg/day without adverse effects.

A CS of 28.7 was calculated based on histological effects in livers and kidneys of rats treated with 5 ppm tin as stannous chloride in the drinking water for life (Schroeder et al., 1968).

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3112 for EPA's Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa and Karen Blackburn were the Technical Project Monitors and John Helms (Office of Toxic Substances) was the Project Officer. The final documents in this series were prepared for the Office of Emergency and Remedial Response, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Office of Air Quality Planning and Standards
Office of Solid Waste
Office of Toxic Substances
Office of Drinking Water

Editorial review for the document series was provided by the following:

Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office
Cincinnati, OH

Technical support services for the document series was provided by the following:

Bette Zwayer, Jacky Bohanon and Kim Davidson
Environmental Criteria and Assessment Office
Cincinnati, OH

TABLE OF CONTENTS

		Page
1.	ENVIRONMENTAL CHEMISTRY AND FATE	1
2.	ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS	4
2.1.	ORAL	4
2.2.	INHALATION	4
3.	TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS	5
3.1.	SUBCHRONIC	5
3.1.1.	Oral	5
3.1.2.	Inhalation	10
3.2.	CHRONIC	10
3.2.1.	Oral	10
3.2.2.	Inhalation	12
3.3.	TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS	12
3.3.1.	Oral	12
3.3.2.	Inhalation	12
3.4.	TOXICANT INTERACTIONS	12
4.	CARCINOGENICITY	13
4.1.	HUMAN DATA	13
4.2.	BIOASSAYS	13
4.2.1.	Oral	13
4.2.2.	Inhalation	14
4.3.	OTHER RELEVANT DATA	15
4.4.	WEIGHT OF EVIDENCE	15
5.	REGULATORY STANDARDS AND CRITERIA	16
6.	RISK ASSESSMENT	17
6.1.	SUBCHRONIC REFERENCE DOSE (RfD_S)	17
6.1.1.	Oral (RfD_{SO})	17
6.1.2.	Inhalation (RfD_{SI})	18

TABLE OF CONTENTS

	Page
6.2. REFERENCE DOSE (RfD)	18
6.2.1. Oral (RfD_O)	18
6.2.2. Inhalation (RfD_I)	20
6.3. CARCINOGENIC POTENCY (q_1^*)	21
6.3.1. Oral	21
6.3.2. Inhalation	21
7. REFERENCES	22
APPENDIX: Summary Table for Tin and Compounds	30

LIST OF ABBREVIATIONS

CAS	Chemical Abstract Service
CS	Composite score
DNA	Deoxyribonucleic acid
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
ppm	Parts per million
RfD	Reference dose
RfD_I	Inhalation reference dose
RfD_O	Oral reference dose
RfD_S	Subchronic reference dose
RfD_{SI}	Subchronic inhalation reference dose
RfD_{SO}	Subchronic oral reference dose
RV_d	Dose-rating value
RV_e	Effect-rating value
TLV	Threshold limit value

1. ENVIRONMENTAL CHEMISTRY AND FATE

Tin is a metallic element that belongs to Group IV A of the periodic table. Tin occurs in the earth's crust as nine different minerals. The most commercially significant ores of tin are cassiterite (SnO_2) and the complex sulfidic ores.

Tin with a valence of +2 and +4 forms stannous [i.e., tin (II)] compounds and stannic [i.e., tin (IV)] compounds. Types of tin compounds include those that contain tin (II) and tin (IV) compounds, complex stannites ($MSnX_3$) and stannates (M_2SnX_6), coordination complexes, organic tin salts where the tin is not bonded through carbon, and organotin compounds, which contain one-to-four carbon atoms bonded directly to tin (Gitlitz and Moran, 1983).

Physical properties of tin and some of its compounds are listed in Table 1-1.

The most environmentally important processes for the degradation of organotin compounds are probably photodegradation with sunlight and microbial degradation. At the levels that organotin compounds are found in the environment, they will eventually be converted to oxides or hydroxides, carbonates or hydrated cations (Blunden and Chapman, 1982). The rate of removal of aliphatic groups from tin compounds reportedly decreases with increasing size of the group, and unsaturated and aromatic groups are cleaved more rapidly (Strand, 1983). In air, tin is commonly found associated with dust particles (Bleier, 1984). The deposition half-life is usually on the order of days for dust particles, depending upon the particle size and characteristics (Nriagu, 1979). Detection of methyl tins in rainwater (Strand, 1933) indicates that these compounds may be removed by

TABLE 1-1

Physical Properties of Tin and Tin Compounds[a]

Compound	CAS Number	Molecular Formula	Atomic or Molecular Weight	Form	Melting Point (°C)	Boiling Point (°C)	Water Solubility (mg/ℓ)
Tin	7440-31-5	Sn	118.69	gray cubic; white rhombic, white metallic tetragonal	232	2260-2270	Insoluble
Tin(IV)dioxide	18282-10-5	SnO_2	150.69	white	1630	sublimes 1800-1900	Insoluble
Tin(II)chloride	7772-99-8	$SnCl_2$	189.60	white	246	652	839,000 (0°C)
Tin(II)sulfate	7488-55-3	$SnSO_4$	214.75	white-yellowish, crystalline powder	decomposes >360	NA	330,000 (25°C)
Tin(II)sulfide	1314-95-0	SnS	150.75	gray-black, cubic, monocyclic	882	1230	0.02 (18°C)
Tin(IV)sulfide	1315-01-1	SnS_2	182.82	gold yellow, hexagonal	decomposes 600	NA	2.0 (18°C)
Tetramethyl tin	594-27-4	$C_4H_{12}Sn$	178.83	colorless liquid	-54[b]	78[b]	Insoluble[b]
Trimethyl tin(IV)chloride	1068-45-1	C_3H_9SnCl	199.24	colorless crystal	37.5[b]	154-156[b]	soluble[b]

[a]All data taken from Weast (1983) unless indicated otherwise

[b]Gilltitz and Moran (1983)

NA = Not available

wet deposition and the volatile organotin compounds may transport long distances. In water, tin has been observed to partition into sediments and bioconcentrate in aquatic organisms (Strand, 1983). Stannous compounds are unstable in dilute aqueous solution.

Above pH 6, stannous solutions oxidize very rapidly. The chemistry of tin (IV) compounds is substantially different. They are stable in solution (Banks, 1969). Environmental methylation of tin may explain the presence of methyl tin compounds in natural water and sediment samples (Rapsomanikis and Weber, 1985). Methylation may result in the formation of volatile tetramethyl tin [vapor pressure 100 mm Hg at 23°C (Perry and Green, 1984], which may account for the worldwide occurrence of methyl tin compounds (Rapsomanikis and Weber, 1985).

Information regarding the environmental chemistry and fate of tin and its compounds in soil could not be located in the available literature.

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

In general, tin compounds are not absorbed well from the gastrointestinal tract. Volunteers in a balance experiment given diets containing 0.11 or 49.67 mg tin (as stannous chloride) daily for 20 days appeared to absorb 50 and 3% of the tin, respectively, as estimated from dietary and fecal tin recovery (Johnson and Greger, 1982). Using tin 113 (a gamma emitter), Hiles (1974) demonstrated that female rats absorbed 2.85 and 0.64% of a single oral dose (20 mg) of either Sn (II) or Sn (IV), respectively. These estimates were based on recovery of radioactivity in the urine and several tissues 48 hours after treatment. Tin compounds tested included tin (II or IV) fluoride, tin (II or IV) citrate, and tin (II) pyrophosphate. Kutzner and Brode (1971) reported that rats and rabbits absorbed <2% of orally administered tin from stannous chloride. Kojima et al. (1978) demonstrated that citric acid or other organic acids can increase the absorption of tin from the gastrointestinal tract of rats.

2.2. INHALATION

Schafer and Femfert (1984) reported that data regarding the absorption of inhaled inorganic tin are limited. There have been reports of the development of stannosis, a benign form of pneumoconiosis resulting from exposure to dust or fumes of tin oxide (Pendergrass and Pryde, 1948; Bartak et al., 1948; Cutter et al., 1949); however, upon examination of tissues from a man with pneumoconiosis who had been exposed occupationally to stannic oxide, Dundon and Hughes (1950) concluded that the amount of tin absorbed from the lungs was insignificant.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

Discussions of toxicity in this document are restricted to tin and its inorganic salts and compounds. The manifestations of toxicity associated with these compounds are similar and suggest that toxicity is due to the tin moiety. There are a number of organotin compounds that will not be discussed because they exhibit markedly different toxic effects, which are not clearly associated with the tin moiety, but are more likely associated with the organic compound per se (ACGIH, 1986).

3.1. SUBCHRONIC

3.1.1. Oral. DeGroot et al. (1972) fed various compounds of tin to weanling Wistar rats for either 4 or 13 weeks. Groups of 10 males and 10 females were fed diets containing 0, 0.03, 0.10, 0.30 or 1.0% of stannic oxide, stannous oxide, stannous orthophosphate, stannous oxalate, stannous sulfide, stannous chloride, stannous sulfate, stannous oleate or stannous tartrate for 28 days. Additional groups of 10 males and 10 females were fed either stannous chloride or stannous oxide in the diet at the levels previously mentioned for 90 days. Endpoints monitored included mortality, growth, food consumption and utilization, hematology, urinalysis, serum biochemistries, and gross and microscopic pathology. No compound-related adverse effects were observed among rats fed stannic oxide, stannous sulfide or stannous oleate for 4 weeks. Anemia and reductions in growth, food consumption and food use efficiency were observed, however, among rats fed either 0.3 or 1% of stannous chloride, orthophosphate, sulfate, oxalate or tartrate; microscopic evidence of liver damage (homogeneous liver cell cytoplasm; slight but definite oval cell type hyperplasia of bile ducts) also was observed in males and females fed 1.0% of the same compounds.

Similar hepatic changes, though of lesser intensity and frequency, were observed among rats fed 0.3% stannous chloride, stannous oxalate or stannous orthophosphate. Females given stannous orthophosphate had a dose-related increase in relative liver weight at ≥0.1%.

No compound-related adverse effects were observed among rats fed stannous oxide for 13 weeks. In the 13-week study with stannous chloride, rats fed 1.0% were killed after 8 weeks on test because of high mortality. Necropsy of these rats revealed anemia, distinct liver changes (described above), severe pancreatic atrophy, enteritis, moderate testicular degeneration, "a spongy state of the white matter of the brain" and acute bronchopneumonia. DeGroot et al. (1972) speculated that some of these changes were due to starvation. Poor appetite and reduced growth were also observed among rats fed 0.3% stannous chloride, but these changes were observed only for the first 2 weeks. Thereafter, growth and food consumption among rats fed 0.3% were similar to controls. Slight anemia (males only) and liver changes (described above) were also observed among rats fed 0.3%. No compound-related adverse effects were observed among rats fed 0.03 or 0.1% stannous chloride for 13 weeks. DeGroot et al. (1972) concluded that 0.1% of tin compounds in the diet (22-33 mg of tin/kg/day; estimated by investigators) was a "no-effect-level."

Fritsch et al. (1977) fed groups of 10 male Sprague-Dawley rats either 0 or 0.5 g tin/100 g (50 ppm) food for 1 month. Stannous chloride was the source of tin. Tin-fed rats had decreased food consumption and growth, marked anemia and marked gastrointestinal irritation.

Dreef-Van Der Meulen et al. (1974) fed groups of 10 male and 10 female weanling Wistar rats diets containing up to 0.8% stannous chloride for 13 weeks. Animals of the test group were accustomed to the ingestion of the

tin by increasing the dietary level from 0.1% in week 1 with weekly increments of 0.1% to a final level of 0.8% (TWA equivalent intake of 246 mg tin/kg/day). Controls were maintained on the basal diet. During the first weeks of the experiment (1-4) when tin levels were low, no distinct differences occurred between test and control groups. Effects attributed to stannous chloride included slight reduction in growth (males only), slight anemia, increased relative liver and kidney weights, gastrointestinal irritation, histologic changes in the liver and pancreatic atrophy. Decreased serum alkaline phosphatase activity, increased relative weights of the heart, adrenals and thyroid, and activated appearance of thyroid follicles were observed among rats fed stannous chloride, but these effects were considered to be of questionable toxicological significance.

Janssen et al. (1985) demonstrated that tin-induced changes in the gastrointestinal tract are independent of food intake. Groups of 10 male Wistar rats were fed 0, 250 or 500 ppm tin (from stannous chloride) for 4 weeks. A fourth group was pair-fed with the 500 ppm tin group. In a second study, groups of four male Wistar rats were fed either 0 or 900 ppm tin (from stannous chloride) for 4 weeks. Dose-related decreases in body weight, food consumption, and food utilization were observed in all tin-fed groups and in the reduced intake (pair-fed) group. The growth reduction in the pair-fed group was comparable with the 500 ppm tin-fed group. Hemoglobin concentrations were also reduced in tin-fed rats. Increased relative weights of the stomach, cecum and colon appeared to be caused by the decrease in body weight, due either to food restriction or to tin feeding. Increased relative weight of small intestine was in part caused by decreased body weight. Comparison of the reduced-diet group and the 500 ppm group suggested that tin feeding resulted in increased absolute weights of the

small intestine. Changes indicative of increased cell turnover (increased migration of epithelial cells along the fillus, formation of ridge-like villi, decreased number of villi per unit surface) were observed in the small intestines of rats fed tin.

DeGroot (1973) examined the effects of dietary iron and copper on the hematological and growth changes caused by stannous chloride in a series of 4- to 6-week studies on weanling Wistar rats. In a 6-week study, groups of 10 males and 10 females were fed 0 or 5300 ppm tin (from stannous chloride) in standard diets or in diets supplemented with copper or iron or both. Significant reduction in growth and hemoglobin levels were observed in rats exposed to tin in the standard diets. Supplementary iron (200 ppm) or copper (75 ppm) or both retarded these effects. In a study where groups of 10 male rats were fed 0, 150, 500 or 1500 ppm tin with or without high levels of copper and iron (10 times the required amount), there were no effects on hemoglobin, serum iron or iron-binding capacity; the only effect was decreased growth in rats in the two higher dose groups. In another 4-week study, groups of 10 males and 10 females were fed 0, 50, 150 or 500 ppm tin (from stannous chloride) in diets that were adequate in copper and either marginally adequate or high in iron. Decreased growth, food consumption and efficiency, hemoglobin and serum iron were observed among rats fed 500 ppm, regardless of the iron content of the diet; however, these effects were more severe among rats fed the diet with marginal iron content. Decreased iron binding capacity was observed among rats fed 500 ppm tin in the diet with marginal iron content. Among rats fed 150 ppm tin, the only effects were reduced hemoglobin in males (both levels of iron) and reduced body weight in females (high iron only). No effects on growth or the blood were observed in rats fed 50 ppm tin with any level of iron in the diet. In

another study, groups of 10 male and 10 female rats were fed either 0 or 150 ppm tin in diets adequate in iron with three different levels of copper for 4 weeks. A decrease in hemoglobin and serum iron levels was observed in rats fed tin and 3 ppm copper and in males fed tin with 6 ppm copper, but not in females fed tin and either 6 or 50 ppm copper or males fed tin with 50 ppm copper.

Yamaguchi et al. (1980) gavaged groups of six weanling male Wistar rats with 0, 0.3, 1.0 or 3.0 mg tin/kg every 12 hours for 90 days. Tin was administered as stannous chloride in an HCl solution. The variables evaluated included enzyme activities in the serum, liver, femur and kidneys, and calcium content of the femur. Rats gavaged with 3.0 mg/kg had significant decreases in relative weight of the femur, calcium content of the femoral diaphysis and epiphysis, calcium concentration, lactic dehydrogenase and alkaline phosphatase activities in the serum, and succinate dehydrogenase activity in the liver. Significantly reduced succinic hydrogenase activity in the liver and significant reductions in calcium content and acid phosphatase activity in the femur were observed among rats gavaged with 1.0 mg/kg. A slight but not significant decrease in the calcium content of the femoral epiphysis was seen in rats treated with 0.3 mg/kg. Yamaguchi et al. (1980) considered 0.6 mg/kg/day (0.3 mg/kg, twice daily) to be the no-effect level.

Yamaguchi et al. (1981) conducted a study with weanling male Wistar rats to assess the effects of tin on bone. Groups of 10 rats were fed diets containing 0, 10, 50, 100 or 250 ppm tin (from stannous chloride) for 90 days. Significant decreases in serum calcium and inorganic phosphate, and in femoral calcium content and acid phosphatase activity were observed in rats fed 100 or 250 ppm. Rats fed 50 ppm tin had significantly reduced serum calcium and femoral calcium. No effects were observed among rats fed 10 ppm.

Savolainen and Valkonen (1986) investigated the effects of stannous chloride on brain and muscular cholinesterase in male Wistar rats. Groups of 30 male rats, averaging 0.365 kg in body weight, were given 0, 0.44 (100 mg/ℓ), 1.11 (250 mg/ℓ) or 2.22 mM (500 mg/ℓ) stannous chloride ($SnCl_2 \cdot 2H_2O$) in drinking water for 1-18 weeks. Groups of five rats were killed and examined after 1, 4, 8, 12, 15 and 18 weeks of treatment. A significant increase in brain acetylcholinesterase activity was observed in the high-dose group after only 1 week of treatment. Dose-related and significant increases in both brain and muscle acetylcholinesterase activity were observed among rats exposed to both 1.11 and 2.22 mM stannous chloride after 18 weeks of treatment. Tin concentration in brain tissue rose steadily over the experimental period.

3.1.2. Inhalation. Data pertaining to subchronic inhalation of tin compounds could not be located in the available literature.

3.2. CHRONIC

3.2.1. Oral. No compound-related effects on growth, survival or histological appearance of tissues were observed among groups of F344 rats or B6C3F1 mice (50/sex/species) fed either 1000 or 2000 ppm stannous chloride in the diet for 105 weeks (NTP, 1982); however, male control mice had significant lower survival than both low- and high-dose male mice (64, 84 and 90% of control, low- and high-dose males survived to the end of the study).

Schroeder and Balassa (1967) gave 5 ppm tin as stannous chloride in the drinking water to Charles River CD mice for life beginning at weaning. Dietary tin concentration was 0.28 ppm. The treated group consisted of 54 males and 54 females. A group of 59 males and 79 females was maintained as controls. There were no compound-related effects on growth, mortality,

grossly examined tissues or histologically examined tissues from hearts, lungs, kidneys, livers and spleens. Although stannous tin accumulated in the spleen and to a lesser extent the heart, no compound-related toxicity was observed.

Schroeder et al. (1968) gave 5 ppm tin as stannous chloride in the drinking water to 56 male and 56 female Long Evans rats for life. The diet contained 0.28 ppm tin. A group of 56 males and 76 females were maintained, though because some experiments involved "general anesthesia and blood letting", some of the rats (~20) were not necropsied. Endpoints evaluated in the study included mortality, growth, longevity, serum glucose, urinary protein and glucose, gross pathology, and microscopic examination of liver, kidney, lungs, heart and spleen. The mean lifespan of females given tin was significantly reduced in comparison with female controls. Tin-fed rats of both sexes had increased incidences of fatty degeneration of the liver (37/80 treated vs. 27/88 controls) and vacuolar changes in the proximal convoluted tubules of the kidney (26/81 treated vs. 16/88 controls).

Roe et al. (1965) conducted an 80-week study with inbred August hooded rats, but interpretation of the results is complicated by changes in dose schedule and the presence of chronic murine pneumonia in most of the rats alive from 1 year to the end of the study. Nursing rats were fed diets containing either no tin or 2% sodium chlorostannate from the time they gave birth until their offspring were weaned. The weanlings were continued on the test diets as follows. Rats whose dams were fed 2% sodium chlorostannate (19 males and 18 females) showed no signs of toxicity at weaning, and were fed 2% sodium chlorostannate in the diet for 7 weeks, the control diet for 4 weeks, then continued on the test diet (2%) for the remainder of the study. A group of 20 males and 20 females was maintained as controls. No nonneoplastic effects were observed in rats fed 2% sodium chlorostannate.

3.2.2. Inhalation. Other than case reports of stannosis (see Chapter 2), data pertaining to chronic inhalation of tin could not be located in the available literature.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. DeGroot et al. (1973) reported moderate testicular degeneration in male Wistar rats fed 1% stannous chloride in the diet for 8 weeks (see Section 3.1.1.).

3.3.2. Inhalation. Data pertaining to the teratogenicity or reproductive toxicity of inhaled compounds of tin could not be located in the available literature.

3.4. TOXICANT INTERACTIONS

Tin affects the homeostasis of essential metals such as copper, iron and zinc. DeGroot (1973) and DeGroot et al. (1972) observed that the anemia and growth retardation observed in rats fed tin-fortified diets could be retarded or inhibited by including high levels of copper or iron (or both) in the diet. Injection of tin and iron into jejunal loops from rats resulted in a decreased absorption of water and iron (Schafer and Forth, 1983). There was no effect of tin on zinc uptake in humans when tin and zinc were given together orally in ratios of 2:1, 4:1 or 8:1, but zinc uptake was inhibited when tin, iron and zinc were administered in ratios of 1:1:1 and 2:1:1 (Solomons et al., 1983). Oral exposure to tin also changed the distribution of copper, iron and zinc in the organs (Greger and Johnson, 1981; Chmielnika et al., 1981; Dwiwedi et al., 1980; Chiba et al., 1984).

4. CARCINOGENICITY

4.1. HUMAN DATA

Data pertaining to the carcinogenic potential of inhaled or ingested tin in humans could not be located in the available literature.

4.2. BIOASSAYS

4.2.1. Oral. NTP (1982) conducted a bioassay on stannous chloride with F344 rats and B6C3F1 mice. Groups of 50 males and females of each species were fed 0, 1000 or 2000 ppm stannous chloride in the diet for 105 weeks. Growth and survival were comparable among all groups of controls and treated animals, except that survival in male control mice was significantly less than that in tin-fed male mice (64, 84 and 98% of the control, low- and high-dose male mice survived to the end of the study). The incidence of C-cell adenomas but not carcinomas of the thyroid was significantly increased in treated male rats in comparison with matched controls (2/50, 9/49, 9/50 in control, low- and high-dose groups, respectively). The combined incidence of C-cell adenomas and carcinomas was significantly elevated above that of the matched controls in both low- and high-dose male rats (2/50, 13/49, 8/50 for controls, low- and high-dose groups, respectively). When the combined incidence of C-cell adenomas and carcinomas in the treated groups are compared with historical controls, the incidence in the low-dose group remains significant but that in the high-dose group does not. The historical control incidence was 11.1% (32/288), 2.3% (8/288) and 8.3% (24/288) for combined adenoma or carcinoma, carcinoma and adenoma, respectively. Since the incidence of C-cell carcinomas or adenomas was not significantly elevated in the high-dose group in comparison with historical controls, and since the incidence of C-cell hyperplasia did not differ among control and treated male rats (control, 1/50; low dose, 1/49; high dose,

2/50), NTP (1982) concluded that stannous chloride did not cause thyroid tumors in either sex of either species. NTP (1982) concluded that stannous chloride is not carcinogenic to either F344 rats or B6C3F1 mice.

NTP (1982) reported that 2-year oral studies conducted by Schroeder et al. (1968) on Long Evans rats and Schroeder and Balassa (1967) on Charles River mice were inadequate to assess the carcinogenicity of stannous chloride since only low levels of compound were tested (0.28 ppm in feed and 5 ppm in water) and since histopathological examination was limited to selected tissues. These studies concluded that stannous chloride was not carcinogenic.

Innes et al. (1969) failed to observe an increased incidence of tumors in mice given triphenyltin acetate by gavage and in the diet for 18 months.

Roe et al. (1965) tentatively concluded that diets containing 2% sodium chlorostannate or 0.5-1% stannous 2-ethyl hexoate were not carcinogenic to inbred August hooded rats (see Section 3.2.1.). Three malignant tumors (mammary adenocarcinoma, uterine pleomorphic sarcoma, adenocarcinoma in the jaw) were observed among 30 rats fed 2% sodium chloroastannate. No neoplasms were observed among 30 controls or among rats that survived for $\geq$1 year on a diet that contained 0.5-1.0% stannous 2-ethyl hexoate. Interpretation of the results of this study, however, are complicated by changes in dose schedule and by the presence of chronic murine pneumonia in most of the rats in the study.

4.2.2. Inhalation. Data pertaining to the carcinogenic potential of inhaled tin could not be located in the available literature.

4.3. OTHER RELEVANT DATA

McLean et al. (1983) demonstrated that tin (II) from stannous chloride, but not tin (IV) from stannic chloride caused alkaline sucrose gradient detectable damage to DNA in Chinese hamster ovary cells. Stannous chloride, stannic chloride and sodium stannate did not induce mutations in repair-deficient strains of Bacillus subtilis (Nishioka, 1975). Triphenyltin acetate and triphenyltin hydroxide did not induce mutations in oral dominant lethal studies on mice (Epstein et al.; 1972).

4.4. WEIGHT OF EVIDENCE

Based on the negative results of the NTP (1982) bioassay in both rats and mice, stannous chloride can be classified in IARC Group 3 or U.S. EPA Group D, i.e., inadequate evidence to refute or demonstrate a carcinogenic potential U.S. EPA (1986) Guidelines for Carcinogen Risk Assessment. While the NTP (1982) concluded that its rat and mice studies did not show a carcinogenic response, this conclusion has some weaknesses. Other bioassays while flawed are not adequate for further evaluation either. The inhalation route has not been evaluated and DNA damage has been shown in one test. These factors combined make the available evidence inadequate to either demonstrate or refute a carcinogenic potential for stannous chloride in humans. Since other compounds of tin have not been tested for carcinogenic potential, tin in general should be classified in U.S. EPA Group D, i.e., not classified as to the human carcinogenic potential

5. REGULATORY STANDARDS AND CRITERIA

OSHA (1985) and ACGIH (1986) recommended a TLV of 2 mg/m³ for occupational exposure to inorganic compounds of tin except stannate (SnH_4). ACGIH (1986) stated that the recommended TLV is designed to protect against stannosis.

6. RISK ASSESSMENT

6.1. SUBCHRONIC REFERENCE DOSE (RfD_S)

6.1.1. Oral (RfD_{SO}). Although several subchronic studies with inorganic tin have been performed DeGroot et al., 1972; Dreef-Van Der Meulen, 1974; Yamaguchi et al., 1980, 1981; Janssen, 1985; Savolainen and Valkonen, 1986), only the studies by DeGroot et al. (1972) and Savolainen and Valkonen (1986) are sufficient for risk assessment. In the study by Savolainen and Valkonen (1986), male Wistar rats (6/group) were given either 0, 100, 250 or 500 mg/ℓ (0, 8.3, 20.8 or 41.6 mg tin/kg/day) stannous chloride in their drinking water for 18 weeks. Tin exposure resulted in a dose-related increase in brain and muscle acetylcholinesterase activity at the two highest doses. There was no effect on brain or muscle acetylcholinesterase activity at the low dose. Weight gain of the exposed rats did not differ from controls at any exposure level. No other parameters were measured. The actual tin content of the food or water (before addition of $SnCl_2$) was not measured. A NOEL of 100 mg/ℓ (8.3 mg tin/kg/day) and a LOAEL of 250 mg/ℓ (20.8 mg/kg/day) were defined in this study.

DeGroot et al. (1972) fed stannous oxide or stannous chloride to groups of 10 male and 10 female Wistar rats at dietary levels of 0, 0.03, 0.1, 0.3 and 1.0% for 90 days. Individual body weights, organ weights, serum chemistry, haematology, urinalysis and gross and microscopic pathology of selected organs were measured. The feeding of stannous oxide at various dietary levels up to 1.0% did not result in any significant changes in any of the parameters examined. Rats fed diets containing 1% stannous chloride showed growth retardation within the first 2 weeks of exposure. Growth was completely stopped by week 4 in males and in females after week 6. Slight anemia, reduced testes weight and liver pathology were observed among rats

fed 0.3% stannous chloride. No compound-related effects were observed among rats fed 0.03 or 0.1% stannous chloride for 13 weeks. The authors concluded that the 0.1% dose level (22-33 mg/kg/day estimated) was a NOEL.

Although the subchronic studies by Savolainen and Valkonen (1986) and DeGroot et al. (1972) are sufficient for risk assessment, the RfD_{SO} derived from either study (0.08 or 0.33 mg/kg/day) would be lower than the value recommended for the RfD_0. Therefore, the RfD_0 of 0.62 mg/kg/day or 43.4 mg/day is recommended for the RfD_{SO}.

6.1.2. Inhalation (RfD_{SI}). There were no data available on the effects of tin inhaled by animals. ACGIH (1986) has recommended TLV of 2 mg/m³ to protect against stannosis. Since there are no appropriate data on the inhalation toxicity of tin, an RfD_{SI} cannot be derived.

6.2. REFERENCE DOSE (RfD)

6.2.1. Oral (RfD_0). Long-term oral animal studies (NTP, 1982; Schroeder et al., 1968) are available for the derivation of an RfD_0 for inorganic tin. In the NTP (1982) study, groups of 50 F344 rats and B6C3F1 mice of each sex were fed diets containing 0, 1000 or 2000 ppm stannous chloride for 105 weeks. No compound-related effects were observed on growth rate, survival or histopathology of tissue at either dose level among tin-fed mice or rats. In the second study (Schroeder et al., 1968), Long-Evans rats (56/sex) were given 5 ppm tin in their drinking water for life. Their diet contained 0.28 ppm tin. Mean lifespan of tin-exposed females was significantly reduced when compared with controls. Tin-exposed rats of both sexes had increased incidences of fatty degeneration of the liver and vacuolar changes in the kidney.

The risk assessment for oral exposure to tin is complicated by several factors. Studies of human dietary intake of tin indicate that ir only fresh meat, cereals and vegetables are eaten, an individual ingests 0.1-1.0 mg tin/kg bw/day (Schroeder et al., 1964; Tipton et al., 1966). If, however, moderate levels of canned fruit juices, fish and vegetables are eaten, dietary intake of tin may reach 38 mg/day (Tipton et al., 1966; Piscator, 1979). Increasing the proportion of canned food in the diet may increase dietary intakes to 500 ppm, equivalent to 14 mg/kg/day, assuming a food factor for humans of 0.028 (U.S. EPA, 1985). An average daily human dietary intake of tin was calculated by Schroeder et al. (1964) to be 4 mg/day. Illness in humans has not been associated with levels of inorganic tin in the diet of 1-38 mg/day (Louria et al., 1972), but acute tin poisoning has been associated with levels $\geq$1370 ppm in individual food items (Schäfer and Femfert, 1984). A level of 250 mg of inorganic tin/kg of canned food is generally accepted as a maximum tolerance level.

An RfD_0 of 38 mg/day or 0.54 mg/kg/day could be derived using the human dietary intake level for tin of 38 mg/day as a NOAEL. Assuming that a large proportion of the population, including subgroups are exposed to this level, no uncertainty factor would be applied. However, because actual exposure to this level is unknown, and because the effects of marginal dietary deficiencies or marked excesses of other nutrients that may interact with tin have not been studied in humans and no long-term human studies are available, an RfD_0 based on dietary levels in humans would be inappropriate.

An RfD_0 could be derived based on the LOAEL of 0.7 mg/kg/day for liver degeneration, vacuolation of renal tubules and decreased survival in rats exposed to 5 ppm tin in their drinking water and 0.28 ppm diet (Schroeder et

al., 1968). The application of an uncertainty factor of 1000 (100 to account for intra- and interspecies extrapolation and 10 for the use of a LOAEL) to the LOAEL would result in an RfD_0 of 0.0007 mg/kg/day or 0.049 mg/day for a 70 kg human. This RfD_0 is questionable as only one dose level was used in the study and several subchronic and chronic studies suggest NOEL and NOAELs at much higher levels in rats, mice and humans.

Using the NOEL of 2000 ppm (62 mg/kg/day) for rats exposed to stannous chloride in the diet for 2 years (NTP, 1982), an RfD_0 of 0.62 mg/kg/day or 43.4 mg/day can be derived by the application of an uncertainty factor of 100. This RfD_0 is further supported by dietary tin intake level of 0.54 mg/kg/day (38 mg/day) at which no adverse effects in humans have been associated.

It is possible to derive a CS for tin. The highest value, 28.7, is derived from the study of Schroeder et al. (1968) on the basis of fatty degeneration of the liver, vacuolization of the renal tubules and decreased longevity in female Long-Evans rats given 5 ppm tin in drinking water (0.7 mg/kg/day) for life. An RV_e of 7 was assigned on the basis of these effects. A higher RV_e was not assigned for decreased longevity since this effect was not reported in rats or mice exposed to 2000 ppm stannous chloride in the diet for 105 weeks (NTP, 1982). An MED of 8.4 mg/day is derived by multiplying the animal dose, 0.7 mg/kg/day, by the product of the cube root of the ratio of animal (0.35 kg) to human reference weight and the human reference weight (70 kg). The MED of 8.4 mg/day corresponds to an RV_d of 4.1. Multiplying the RV_d by the RV_e yields a CS of 28.7.

6.2.2. Inhalation (RfD_I). There were no data available on the inhalation of tin in animals; therefore, an RfD_I for tin cannot be derived. A TLV of 2 mg/m³ by ACGIH (1986) and OSHA (1985 has been recommended.

ACGIH (1986) did not report how this particular level of exposure was determined, but it is intended to be protective of stannosis.

6.3. CARCINOGENIC POTENCY

6.3.1. Oral. Since compounds of tin have inadequate evidence from which to assess the human carcinogenic potential (NTP, 1982; Innes et al., 1969), no potency factor is derived.

6.3.2. Inhalation. Since there were no data available on the carcinogenic potential of inhaled tin, no potency factor is derived.

7. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH. p. 574.

Banks, C.K. 1969. Tin compounds. In: Kirk-Othmer Encyclopedia of Chemical Technology, 2nd ed., Vol. 20, A. Standen, Ed. John Wiley and Sons, Inc., New York. p. 309.

Bartak, F., M. Tomecka and O. Tomisek. 1948. Stanniosis (pneumoconiosis due to tin). Cas. Lek. Cesk. 87: 915-292. (Cited in Schafer and Femfert, 1984)

Bleier, A. 1984. Colloids. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed., Vol. Supplement, M. Grayson and D. Eckroth, Ed. John Wiley and Sons, Inc., New York. p. 252.

Blunden, S.J. and A.H. Chapman. 1982. The environmental degradation of organotin compounds. A review. Sci. Technol. Lett. 3: 267-272.

Chiba, M., K. Ogihara, Y. Inaba, T. Nishima and M. Kikuchi. 1984. The organ distribution of tin and the effect of tin on concentrations of several essential elements in rabbit. Toxicology. 31(1): 23-32.

Chmielnicka, J., J.A. Szymanska and J. Sniec. 1981. Distribution of tin in rats and disturbances in the metabolism of zinc and copper due to repeated exposure to $SnCl_2$. Arch. Toxicol. 47: 263-268. (Cited in Schafer and Femfert, 1984)

Cutter, H.C., W.W. Faller, J.B. Stocklen and W.L. Wilson. 1949. Benign pneumoconiosis in a tin oxide recovery plant. J. Ind. Hyg. 31: 139-141. (Cited in Shafer and Femfert, 1984)

DeGroot, A.P. 1973. Subacute toxicity of inorganic tin as influenced by dietary levels of iron and copper. Food Cosmet Toxicol. 11(6): 955-962.

DeGroot, A.P., V.J. Feron and H.P. Til. 1972. Short-term toxicity studies on some salts and oxides of tin in rats. Food Cosmet. Toxicol. 11(1): 19-30.

Dreef-Van der Meulen, H.C., V.J. Feron and H.P. Til. 1974. Pancreatic atrophy and other pathological changes in rats following the feeding of stannous chloride. Pathol. Eur. 9(3): 185-192.

Dundon, C.C. and J.P. Hughes. 1950. Stannic oxide pneumoconiosis. Am. J. Roentgenol. Radium Ther. 63: 797-812. (Cited in Schafer and Femfert, 1984)

Dwiwedi, R.S., G. Kaur, R.K. Jaiswal and R.C. Srivastava. 1980. The effect of metals salts on the distribution of iron-59 in rats: Manganese (II), nickel (II) and tin (II). Acta Pharmacol. Toxicol. 47: 33-37. (Cited in Schafer and Femfert, 1984)

Epstein, S., E. Arnold, J. Andrea, W. Bass and Y. Bishop. 1972. Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23: 288-325. (Cited in U.S. EPA, 1979)

Fritsch, P., B.G. DeSaint and R. Derache. 1977. Nutritional and toxicological study of rats fed a diet containing tin. Toxicology. 8(2): 165-175. (French with English abstract)

Gitlitz, M.H. and M.K. Moran. 1983. Tin compounds. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed., Vol. 23, M. Grayson and D. Eckroth, Ed. John Wiley and Sons, Inc., New York. p. 42, 53.

Greger, J.L. and M.A. Johnson. 1981. Effect of dietary tin on zinc. Copper and iron utilization in rats. Food Cosmet Toxicol. 19(2): 163-166.

Hiles, R.A. 1974. Absorption, distribution and excretion of inorganic tin in rats. Toxicol. Appl. Pharmacol. 27(2): 366-379.

Innes, J., B. Ulland, M. Valerio, et al. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. J. Natl. Cancer Inst. 42: 1101-1114. (Cited in U.S. EPA, 1979)

Janssen, P.J., M.C. Bosland, J.P. van Hees, B.J. Spit, M.I. Williams and C.F. Kuper. 1985. Effects of feeding stannous chloride on different parts of the gastrointestinal tract of the rat. Toxicol. Appl. Pharmacol. 78(1): 19-28.

Johnson, M.A. and J.L. Greger. 1982. Effects of dietary tin on tin and calcium metabolism of adult males. Am. J. Clin. Nutr. 35(4): 655-660.

Kojima, S., K. Saito and M. Kiyozumi. 1978. Studies on poisonous metals: IV. Absorption of stannic chloride from rat alimentary tract and effect of various food components on its absorption. Yabugakw Zasshi. 98: 495-502. (Cited in Schafer and Femfert, 1984)

Kutzner, J. and K.H. Brode. 1971. Resorption and excretion of tin after oral administration of tin-113. Nucl. Med. 10(3): 286-297. (German with English abstract)

Louria, D.B., M.M. Joselow and A.A. Browder. 1972. Human toxicity of certain trace elements. Ann. Intern. Med. 76: 307-319.

McLean, J.R.N., D.H. Blakey, G.R. Douglas and J.G. Kaplan. 1983. The effect of stannous and stannic (tin) chloride on DNA in Chinese hamster ovary cells. Mutat. Res. 119(2): 195-201.

Nishioka, H. 1975. Mutagenic activities of metal compounds in bacteria. Mutat. Res. 31: 185-189. (Cited in U.S. EPA, 1979)

Nriagu, J.O. 1979. Copper in the atmosphere and precipitation. In: Copper Environment, J.O. Nriagu, Ed. John Wiley and Sons, NY. p. 43-75.

NTP (National Toxicology Program). 1982. Carcinogenesis bioassay of stannous chloride (CAS No. 7772-99-8) in F344/N rats and B6C3F1/N mice (feed study). NCI/NTP Tech. Rep. Ser. No. 231. (Also published as DHHS (NIH) publ. Iss NIH 82-1787 and NTIS PB 82-242-553) p. 149.

OSHA (Occupational Safety and Health Administration). 1985. OSHA Occupational Standards: Permissible Exposure Limits. 29 CFR 1910.1000.

Pendergrass, E.P. and A.W. Pryde. 1948. Benign pneumoconiosis due to tin oxide. J. Ind. Hyg. Toxicol. 30: 119-123. (Cited in Schafer and Femfert, 1984)

Perry, R.H. and D. Green, Ed. 1984. Perry's Chemical Engineers' Handbook, 6th ed. McGraw-Hill Book Co., New York. p. 3-49.

Piscator, M. 1979. In: Handbook on the Toxicology of Metals, L. Friberg, G. Nordberg and V.B. Vouk, Ed. Elsevier, North Holland, Amsterdam, New York. (Cited in Schafer and Femfert, 1984; Underwood, 1977)

Rapsomanikis, S. and J.H. Weber. 1985. Environmental implications of methylation of tin (II) and methytin (IV) ions in the presence of manganese dioxide. Environ. Sci. Technol. 19: 352-356.

Roe, F.J., E. Boyland and K. Millican. 1965. Effects of oral administration of two tin compounds to rats over prolonged periods. Food Cosmet. Toxicol. 3(2): 277-280.

Savolainen, H. and S. Valkonen. 1986. Dose-dependent brain tin concentration in rats given stannous chloride in drinking water. Toxicol. Lett. 30(1): 35-39.

Schafer, S.G. and U. Femfert. 1984. Tin -- A toxic heavy metal? A review of the literature. Regul. Toxicol. Pharmacol. 4(1): 57-69.

Schafer, S.G. and W. Forth. 1983. The influence of tin, nickel and cadmium on the intestinal absorption of iron. Ecotoxicol. Environ. Saf. 7: 87-95. (Cited in Schafer and Femfert, 1984)

Schroeder, H. and J. Balassa. 1967. Arsenic, germanium, tin and vanadium in mice. Effects on growth, survival and tissue levels. J. Nutr. 92: 245-252.

Schroeder, H.A., J.J. Balassa and I.H. Tipton. 1964. Abnormal trace elements in man. Tin. J. Chron. Dis. 17: 483-502. (Cited in Schafer and Forth, 1983)

Schroeder, M., M. Kanisawa, D. Frost and M. Mitchener. 1968. Germanium, tin and arsenic in rats: Effects on growth, survival, pathological lesions and lifespan. J. Nutr. 96: 37-45.

Schwartz, K., D.B. Milne and E. Vinyard. 1970. No title provided. Biochem. Biophys. Res. Commun. 40: 22. (Cited in Underwood, 1977)

Solomons, N.W., J.S. Marchini, R.M. Duarte-Favaro, H. Vannuchi and J.E. Dutra de Oliveira. 1983. Studies on the bioavailability of zinc in humans: Intestinal interaction of tin and zinc. Am. J. Clin. Nutr. 37(4): 566-571.

Strand, J.A. 1983. Biological fate and effects of organotin compounds in the marine environment. TR83-1 Seattle, Washington. Nav. Reserve Cent. NTIS AD-A133890. 23 p.

Tipton, I., P.L. Stewart and P.G. Martin. 1966. Trace elements in diets and excreta. Health Phys. 12: 1683-1689. (Cited in Schafer and Femfert, 1984)

Underwood, E.J. 1977. Trace Elements in Human and Animal Nutrition, 4th ed. Academic Press, NY. 345 p.

U.S. EPA. 1979. Mini-Reviews on the Carcinogenicity, Mutagenicity and Chronic Toxicity of Selected Compounds. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

U.S. EPA. 1980. Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Quality Criteria Documents. Federal Register. 45(231): 49347-49357.

U.S. EPA. 1983. Methodology and Guidelines for Reportable Quantity Determinations Based on Chronic Toxicity Data. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1985. Reference Values for Risk Assessment. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

U.S. EPA. 1986. Guidelines for Carcinogenic Risk Assessment. Federal Register. 51(185): 33992-34003.

Weast, R.C., Ed. 1983. CRC Handbook of Chemistry and Physics, 64th ed. CRC Press Inc., Boca Raton, FL. p. B-150, B-151.

Yamaguchi, M., R. Saito and S. Okada. 1980. Dose-effect of inorganic tin on biochemical indices in rats. Toxicology. 16(3): 267-273.

Yamaguchi, M., K. Sugii and S. Okada. 1981. Inorganic tin in the diet affects the femur in rats. Toxicol. Lett. 9(3): 207-209.

APPENDIX

Summary Table for Tin and Compounds

	Species	Experimental Exposure/Dose	Effect	Reference Dose RfD or RfD_S (mg/day)	Reference
Inhalation					
RfD_{SI} (formerly AIS)	human	2 mg/m³ occupational (0.204 mg/kg/day)	none	1.4	ACGIH, 1986
RfD_I (formerly AIC)	human	2 mg/m³ occupational (0.204 mg/kg/day)	none	1.4	ACGIH, 1986
Oral					
RfD_{SO}	human	30 mg/day contribution from diet	none	43.4	NTP, 1982
RfD_O	human	30 mg/day contribution from diet	none	43.4	NTP, 1982
Maximum					
CS	rat (f)	5 ppm $SnCl_2$ in water and 0.28 ppm Sn in diet for life (0.7 mg/kg/day) RV_d = 4.1	fatty degeneration of the liver; vacuolization of renal tubules RV_e = 7	28.7	Schroeder et al., 1968